PATENT

ISIS-1158

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:

Nielsen, et al.

Serial No.: 08/319,411 Group Art Unit: 1631

Filed: October 6, 1994 Examiner: A. Marschel

For: PEPTIDE NUCLEIC ACID CONJUGATES

I, John A. Harrelson, Jr., Registration No. 42,637 certify that this correspondence is being deposited with the U.S. Postal Service as First Class mail in an envelope addressed to the Assistant Commissioner for Patents, Washington, D.C. 20231.

On March 20, 2002

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Assistant Commissioner for Patents
Washington, D.C. 20231

APPELLANT'S BRIEF PURSUANT TO 37 C.F.R. § 1.192

Applicants appeal the Final Rejection dated August 29, 2001 in connection with the above-identified application.

I. Real Party in Interest

Based on information supplied by Applicants and to the best of the undersigned's knowledge, the real parties in interest in the above-identified patent application are Peter Nielsen, who is the assignee of Soren Holst Sonnichsen and Jesper Lohse; Ole Buchardt; Michael Egholm; and ISIS Pharmaceuticals, Inc., a corporation of Delaware, which is the assignee of Muthiah Manoharan, John Kiely, Michael Griffith, and Kelly Sprankle.

II. Related Appeals and Interferences

There are no other appeals or interferences known to Appellants, Appellants' legal representative, or the assignee that will directly affect or be directly affected by or have a bearing on the Board's decision in the pending Appeal.

III. Status of Claims

Claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37, and 39-52 are pending in this patent application and are the subject of this Appeal. These claims appear in Appendix A.

IV. Status of Amendments

No amendments have been made since the issuance of the Final Rejection.

V. Summary of the Invention

The present invention is directed to a novel class of peptide nucleic acids that include a conjugate attached thereto (Specification at page 13, lines 27-28.) The peptide nucleic acids generally comprise ligands such as naturally occurring DNA bases attached to a peptide backbone directly or through suitable linkers (Claim 1). As shown in claim 5, suitable conjugates include a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers. These compositions are useful as, for example, pharmaceutical agents (Specification at page 15, lines 25-29.)

VI. Issues

This appeal seeks to resolve 11 issues:

1. whether or not the Examiner has demonstrated that the subject matter of claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37, 39-43, 45, 46, 48, and 50 would have been obvious to those of ordinary skill in the art in view of the disclosure of U.S. Patent No. 5,705,333;

2. whether or not the Examiner has demonstrated that the subject matter of claims 8-10, 15, 20, 22-24, 30-33, 37, 40, 41, and 45-50 would have been obvious to those of ordinary skill in the art in view of the disclosure of U.S. Patent No.5,623,049;

3. whether or not the Examiner has demonstrated, in accordance with the judicially-created doctrine of obviousness-type double patenting, that those of ordinary skill in the art would have regarded the subject matter of claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37, 39-43, and 45-52 as an obvious variant of the subject matter of claims 1-3 of U.S. Patent 5,539,082;

4. whether or not the Examiner has demonstrated, in accordance with the judicially-created doctrine of obviousness-type double patenting, that those of ordinary skill in the art would have regarded the subject matter of claims 1, 5, 8-10, 12, 13, 15, 20, 37, 39-41, 47-49, 51, and 52 as an obvious variant of the subject matter of claim 1 of U.S. Patent 5,773,571;

5. whether or not the Examiner has demonstrated, in accordance with the judicially-created doctrine of obviousness-type double patenting, that those of ordinary skill in the art would have regarded the subject matter of claim 50 as an obvious variant of the subject matter of claims 1, 5, and 8 of U.S. Patent 5,786,461;

6. whether or not the Examiner has demonstrated, in accordance with the judicially-created doctrine of obviousness-type double patenting, that those of ordinary skill in the art would have regarded the subject matter of claims 8-10, 15, 20, 30-33, 37, 40, 41, 47-49, 51 and 52 as an obvious variant of the subject matter of claims 1 and 9 of U.S. Patent 5,719, 262;

7. whether or not the Examiner has demonstrated, in accordance with the judicially-created doctrine of obviousness-type double patenting, that those of ordinary skill in the art would have regarded the subject matter of claims 8-10, 15, 20, 30-33, 37, 40, 41, 47-49, 51, and 52 as an obvious variant of the subject matter of claims 4, 5, 9, and 40 of copending application Serial No. 08/108,591;

8. whether or not the Examiner has demonstrated, in accordance with the judicially-created doctrine of obviousness-type double patenting, that those of ordinary skill in the art would have regarded the subject matter of claims 1, 5, 8-10, 12, 13, 15, 20, 37, 39-41, 47-49, 51, and 52 as an obvious variant of the subject matter of

claims 2, 6, 7, 9, 22, 24, 25, 27, 35, 37-39, and 44 of copending application Serial No. 08/275,951 in view of Switzer, *et al., Bioch.* **1993**, *32*, 10489;

9. whether or not the Examiner has demonstrated, in accordance with the judicially-created doctrine of obviousness-type double patenting, that those of ordinary skill in the art would have regarded the subject matter of claims 1, 5, 8-10, 15, 20, 30-33, 37, 40, 41, 47-49, 51, and 52 as an obvious variant of the subject matter of claims 1, 5, and 13 of copending application Serial No. 08/686,114 taken in view of International Patent Application PCT U.S. 86/05518;

10. whether or not the Examiner has demonstrated, in accordance with the judicially-created doctrine of obviousness-type double patenting, that those of ordinary skill in the art would have regarded the subject matter of claims 1, 5, 8-10, 12, 13, 15, 20, 37, 39-41, 47-49, 51, and 52 as an obvious variant of the subject matter of claims 2, 6, 7, 34, 35, 38, 40, and 42 of copending application Serial No. 08/765,798 in view of Switzer, *et al., Bioch.* **1993**, *32*, 10489; and

11. whether or not the Examiner has demonstrated, in accordance with the judicially-created doctrine of obviousness-type double patenting, that those of ordinary skill in the art would have regarded the subject matter of claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37, 39-52 as an obvious variant of the subject matter of claims 24, 26, and 28 of copending application Serial No. 09/106,667.[1]

VII. Grouping of the Claims

Given the nature of the Examiner's rejection of claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37, 39-43, 45, 46, 48, and 50 under 35 U.S.C. § 103 (a) based on the U.S. Patent 5,705,333, Applicants believe that claim 1 stands alone and that the other claims stand or fall together. Applicants believe that claim 1 stands alone in view of admissions in prior Office Actions (discussed below) that have specific relevance to the patentability of claim 1.

For each other ground of rejection which applies to a group of two or more claims, the remaining claims are believed to stand or fall together within their respective groups.

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[1] Applicants note that they have not appealed the rejection of claims 22-24, 45, 46, and 50 for alleged obviousness-type double patenting in view of claims 8, 34, 35, 37, 40-47, 49-51, 53-56, 61-63, 66-69, 71-76, and 89-93 of copending application Serial No. 08/468,719. Upon resolution of the other outstanding issues, Applicants

VIII. Argument

1. The Rejection Under 35 U.S.C. § 103(a) in View of the 333 Patent Is Improper

The rejection of claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37, 39-43, 45, 46, 48, and 50 under 35 U.S.C. § 103(a) in view of U.S. Patent No. 5,705,333 ("the 333 Patent") is improper for at least two reasons: (1) the 333 Patent is not prior art with respect to the claimed inventions; and (2) even if it were prior art, there is no evidence of record suggesting that it would have motivated those of ordinary skill to make or use a claimed invention. In addition, admissions in prior Office Actions indicate that this rejection is procedurally improper at least as to claim 1.

That the 333 Patent is not prior art against the instant invention is revealed by a comparison of the patent's disclosure with that of Applicants' priority application, U.S. Patent Application No. 08/108,591 ("the 591 Application"). Although the Examiner suggests that rejection of the present claims is appropriate because the 591 Application allegedly shows attachment of conjugates to the claimed compounds only at terminal sites (August 29, 2001 Final Rejection at page 3), this clearly is not the case. For example, the 591 Application states at page 15, lines 32-35, that conjugates (such as DNA intercalators or reporter ligands) can be attached to the claimed compounds at position "L" which, as shown in Figure 1 on page 8, constitutes an intermediate – rather than terminal (*i.e.*, end) -- position in the claimed compounds (*see also*, page 17, lines 13-27 of the 591 Application, wherein Applicants teach that conjugates can be effector ligands such as reporter ligands, water-soluble polymer, enzymes, ligands with nuclease activity, or alkylating agents). This disclosure directly refutes the Examiner's allegations regarding the teaching of the 591 Application, and thereby enables Applicants – through their claim of priority -- to antedate the 333 Patent, which was filed over eight months after the November 22, 1993 filing date of the 591 Application.[2]

Even if the 333 Patent were properly applied against the instant claims, there is no evidence of record indicating that persons of ordinary skill would have found the instant claims obvious. Although the Office Action alleges that the peptide backbones of the instant invention

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are prepared to file a terminal disclaimer with respect to these claims, either in the present patent application or in a continuing patent application, to remove this rejection.

[2] Withdrawal of the rejection is particularly warranted as to claim 1, because the Examiner does not dispute that the subject matter it claims is fully supported by the 591 Application. Claim 1 is directed to compounds in which a conjugate is bound to at least one end of the compound's backbone, and the Examiner acknowledges that the 591 Application shows conjugates at terminal positions (August 29, 2001 Office Action at page 3). As such, the rejection is improper and should be withdrawn.

are a species of the backbones described in the 333 Patent (November 27, 2000 Office Action at pages 4-5), the presence of a claimed species within a genus disclosed by the prior art is not sufficient by itself to establish a *prima facie* case of obviousness. *In re Baird*, 29 U.S.P.Q.2d 1550 (Fed. Cir. 1994); MPEP § 2144.08, II; *In re Jones,* 958 F.2d 347, 350, 21 U.S.P.Q.2D (BNA) 1941, 1943 (Fed. Cir. 1992) (rejecting Commissioner's argument that "regardless [] how broad, a disclosure of a chemical genus renders obvious any species that happens to fall within it"). There still must be a teaching that would have motivated one of ordinary skill in the art to make a claimed compound based on the 333 Patent's disclosure. *In re Fine*, 837 F.2d 1071, 1074, 5 U.S.P.Q.2D (BNA) 1596, 1598 (Fed. Cir. 1988) (obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art.); M.P.E.P. § 2143.01, 3¶.

The Examiner has failed to identify any teaching that would have motivated modifying the prior art in a way that would have led to a claimed invention. In an attempt to show overlap between the instant claims and the 333 Patent disclosure, the Examiner has proffered a table that he has been able construct with the benefit of hindsight by selecting certain groups from the many possibilities recited in one section of the 333 Patent (November 27, 2000 Office Action at page 7). Although the Examiner alleges that it would have been obvious to modify the "composite structure" recited in the table by including one of the functional groups that are taught in a different section of the patent (November 27, 2000 Office Action at page 7), much more is required to establish obviousness. Indeed, the Examiner has failed to provide any reason, other than a mere allegation that the 333 Patent describes species of the instant invention (November 27, 2000 Office Action at page 9), why a person of ordinary skill would have been motivated to make the selections necessary to yield the composite structure or, having made such selections, to modify that structure. As discussed above, it is only with hindsight that such species can be selected. Thus, the rejection for alleged obviousness is improper. *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453, 1457-58 (Fed. Cir. 1998) ("To prevent the use of hindsight based on the invention to defeat patentability of the invention, this court requires the examiner to show motivation to combine the references that create the case of obviousness.").

The Examiner is mistaken with respect to his allegation (October 27, 2000 Office Action at page 7) that a compound that he has identified in the 333 Patent would be within the scope of Applicants' claims. As will be noted, claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37, 39-43, 45, 46, 48, and 50 require that a compound according to the invention include at least ***two*** moieties -- a nucleobase and a conjugate. The Examiner's composite structure, however, includes only a ***single*** moiety (*i.e.*, nucleobase) that is alleged to serve as both a nucleobase and a conjugate (November 27, 2000 Office Action at page 5). Thus, the compounds would be outside the scope of the instant claims. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974) (all limitations set forth in a patent claim must be taught or suggested in the prior art to establish obviousness). Since the Examiner's proposed modification of the 333 Patent's disclosure would not produce any claimed invention, the rejection for alleged obviousness should be withdrawn.

2. The Rejection Under 35 U.S.C. § 103(a) in View of the 049 Patent Is Improper

There are also at least two reasons why the rejection of claims 8-10, 15, 20, 22-24, 30-33, 37, 40, 41, and 45-50 under 35 U.S.C. § 103(a) in view of U.S. Patent 5,623,049 ("the 049 Patent") is improper: (1) the 049 Patent is not prior art with respect to the claimed inventions; and (2) even if it were prior art, there is no evidence of record suggesting that it would have motivated those of ordinary skill to make or use a claimed invention.

First, as noted above, the effective filing date of the appealed claims is November 22, 1993 (based on the 591 Application), which is over nine months before the earliest effective filing date of the 049 Patent. Thus, the 049 Patent cannot properly be applied to support a rejection under Section 103.

Second, even if the 049 Patent were properly applied against the instant claims, there is no evidence of record indicating that persons of ordinary skill would have found the claimed subject matter obvious. Although the Office Action alleges that the 049 Patent discloses the claimed structures (November 27, 2000 Office Action at page 9), this assertion is incorrect. As will be noted, claims 8-10, 15, 20, 22-24, 30-33, 37, 40, 41, and 45-50 require that a compound according to the invention include at least ***two*** moieties -- a nucleobase and a conjugate. The Office Action alleges that, in the 049 Patent, lysine serves as both a nucleobase and a cross-linker (a type of conjugate) and thus constitutes a conjugate of the instant invention. (November 27, 2000 Office Action at page 9.) However, in the 049 Patent's lysine-containing structure, only a ***single*** moiety (*i.e.*, lysine) is alleged to serve as both a nucleobase and a conjugate. Thus,

the proffered compound is outside the scope of the instant claims. Because the Examiner's proposed selection from the 049 Patent's disclosure would not correspond to any claimed invention, the rejection for alleged obviousness should be withdrawn. *In re Royka*, 490 F.2d 981, 180 U.S.P.Q. 580 (C.C.P.A. 1974) (all limitations set forth in a patent claim must be taught or suggested in the prior art to establish obviousness).

2. The Rejections Based on Obviousness-Type Double Patenting Are Not Proper

a. The Rejection Based on the 082 Patent Is Not Proper

Claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37, 39-43, and 45-52 are rejected under the judicially created doctrine of obviousness-type double patenting in view of claims 1-3 of U.S. Patent 5,539,082 ("the 082 Patent") because the constituent nucleobases of the PNA compounds disclosed by the 082 Patent allegedly qualify as cross-linkers according to Applicants' invention. However, there is no evidence of record so much as suggesting that the nucleobases disclosed by the 082 Patent would function as cross-linkers. In the absence of such evidence, the rejection should be withdrawn.

b. The Rejections Based on the 571 Patent, the 461 Patent, the 262 Patent, the 591 Application, 114 Application In View of the Summerton Reference and the 667 Application Are Not Proper

Claims 1, 5, 8-10, 12, 13, 15, 20, 22-24, 30-33, 37, and 39-52 stand rejected under the judicially created doctrine of obviousness-type double patenting in view of one of more of: U.S. Patent No. 5,773,571 ("the 571 Patent"), 5,786,461 ("the 461 Patent"), and 5,719, 262 ("the 262 Patent"), and patent application Serial Nos. 08/108,591 ("the 591 Application"), and 09/106,667 ("the 667 Application"). In addition, claims 1, 5, 8-10, 15, 20, 30-33, 37, 40, 41, 47-49, 51, and 52 stand rejected for alleged obviousness-type double patenting over application Serial No. 08/686,114 ("the 114 Application") taken in view of International Patent Application PCT U.S. 86/05518 ("the Summerton reference"). The basis for these rejections, as with the above-noted rejection over the 082 Patent claims, is that the constituent nucleobases of the PNA compounds disclosed by the cited patents allegedly qualify as cross-linkers according to Applicants' invention. Because there is no evidence of record suggesting that the nucleobases disclosed by the claims of these patents would function in this manner, Applicants respectfully request that the rejections be withdrawn.

c. The Rejection Based on the 951 Application In View of the Switzer Reference Is Not Proper

Claims 1, 5, 8-10, 12, 13, 15, 20, 37, 39-41, 47-49, 51, and 52 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 2, 6, 7, 9, 22, 24, 25, 27, 35, 37-39, and 44 of copending application Serial No. 08/275,951 ("the 951 Application") taken in view of Switzer, *et al., Bioch.* **1993**, *32*, 10489 ("the Switzer reference"). The basis for this rejection is that those of ordinary skill in the art allegedly would have been motivated to use the polymerase enzymes disclosed by the Switzer reference with the peptide nucleic acid (PNA) compounds recited in the 951 Application claims. The teaching of the Switzer reference, however, is limited to the use of polymerases with duplex ***oligonucleotides*** (*see* the Switzer reference Abstract, page 10489), and the reference does not so much as mention PNAs such as those recited in the claims. Since the Examiner has not identified any reason why those of ordinary skill would have been motivated to modify the 951 Application claims in the manner proposed, the double patenting rejection based on the 951 application is improper.

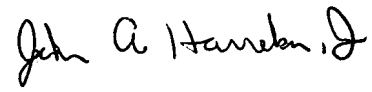
d. The Rejection Based on the 798 Application In View of the Switzer Reference Is Not Proper

Claims 1, 5, 8-10, 12, 13, 15, 20, 37, 39-41, 47-49, 51, and 52 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 2, 6, 7, 34, 35, 38, 40, and 42 of copending application Serial No. 08/765,798 ("the 798 Application") taken in view of the Switzer reference. The basis for this rejection, as with the above-noted rejection over the 951 Application claims, is that those of ordinary skill in the art allegedly would have been motivated to use the polymerase enzymes disclosed by the Switzer reference with the PNA compounds recited in the 798 Application claims. As with the 951 Application, however, the Examiner has not identified any motivation to apply the Switzer reference's teachings relating to oligonucleotides to the PNA compounds recited in the 798 Application claims. Accordingly, the rejection for alleged obviousness-type double patenting is improper.

IX. Conclusion

For the foregoing reasons, Applicants request that this patent application be remanded to the Patent Office with an instruction to both withdraw the outstanding rejections and allow the appealed claims.

Respectfully submitted,



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Serial No.: 08/319,411 **Group Art Unit: 1631**

Filed: October 6, 1994 **Examiner: A. Marschel**

For: PEPTIDE NUCLEIC ACID CONJUGATES

Assistant Commissioner for Patents
Washington, D.C. 20231

APPENDIX A TO APPELLANTS' BRIEF

1. A peptide nucleic acid conjugate comprising:

a peptide nucleic acid;

said peptide nucleic acid having a backbone;

said backbone having an amino end, a carboxyl end, a plurality of amino groups, and a conjugate bound directly or through a linking moiety to at least one of said amino end or said carboxyl end;

said amino groups each having a tethered nucleobase; and

said conjugate being a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator;

wherein said crosslinking agent is not lysine.

5. A peptide nucleic acid conjugate comprising:

a peptide nucleic acid;

said peptide nucleic acid having a backbone;

said backbone having an amino end, a carboxyl end, and a plurality of amino groups;

said amino groups each having a tethered nucleobase and a conjugate bound to said nucleobase or said tether either directly or through a linking moiety, wherein said conjugate is a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers.

8. A peptide nucleic acid conjugate of claim 37 wherein said conjugate includes a linking moiety.

9. A peptide nucleic acid conjugate of claim 37 wherein at least one group R^{12} is a conjugate.

10. A peptide nucleic acid conjugate of claim 37 wherein at least one of L and L_m is $R^{12}(R^{13})_l$ is a conjugate.

12. A peptide nucleic acid conjugate of claim 39 wherein at least one of said $A\text{-}A_m$ groups include at least one of R^1, R^2, and R^3.

13. A peptide nucleic acid conjugate of claim 39 wherein at least one of $B\text{-}B_m$ groups or said $G\text{-}G_m$ groups include at least one group R^3.

15. A peptide nucleic acid conjugate of claim 37 wherein at least one of said groups Q or I include at least one of groups R^8, R^9, R^{10}, and R^{11}.

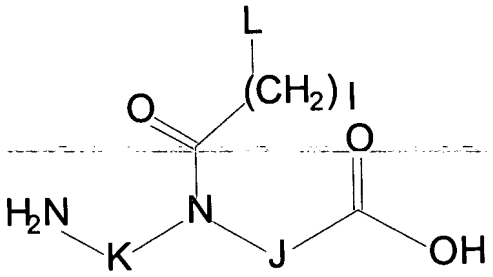
20. A peptide nucleic acid conjugate of claim 37 wherein m is from 1 to about 20.

22. A peptide nucleic acid conjugate of claim 50 wherein said conjugate includes a linking moiety.

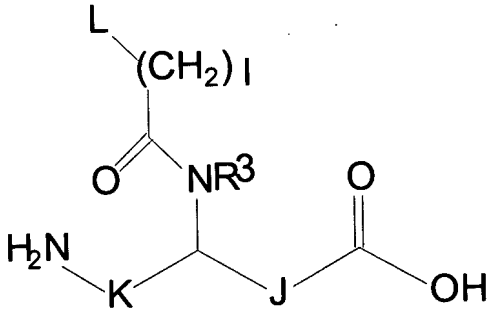
23. A peptide nucleic acid conjugate of claim 50 wherein R^{12} is a conjugate.

24. A peptide nucleic acid conjugate of claim 50 wherein a is 1.

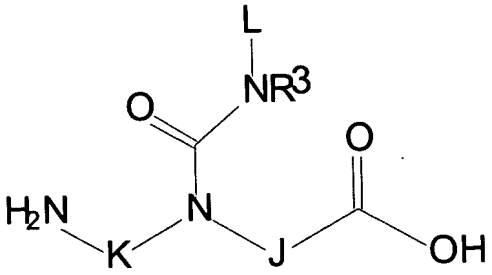
30. A peptide nucleic acid conjugate oligomer comprising a plurality of covalently linked PNA monomers wherein at least one of said PNA monomers has the formula:



or the formula



or the formula



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, (C_1-C_4)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13}, if present, is a conjugate; and

a is 0 or 1;

K is $(CR^6R^7)_z$;

J is $(CR^6R^7)_y$; wherein:

R^6 and R^7 are independently hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4) alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio or amino;

R^5 is hydrogen, a conjugate, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C_1-C_6)alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

l is an integer from 1 to 5; and

at least one of L and R^3 comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

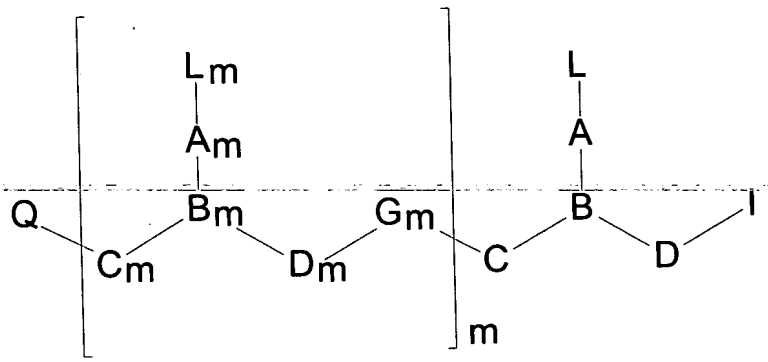
wherein said conjugate optionally includes a linking moiety.

31. A peptide nucleic acid conjugate of claim 30 wherein said conjugate includes a linking moiety.

32. A peptide nucleic acid conjugate of claim 30 wherein R^{12} is a conjugate.

33. A peptide nucleic acid conjugate of claim 30 wherein a is 1.

37. A peptide nucleic acid conjugate of the formula:



wherein:

m is an integer from 1 to about 50;

L and L_m independently are $R^{12}(R^{13})_a$ wherein:

R^{12} is hydrogen, hydroxy, $(C_1\text{-}C_4)$alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate;

provided that at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13}, if present, is a conjugate; and

a is 0 or 1;

C and C_m independently are $(CR^6R^7)_y$; wherein:

R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2\text{-}C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1\text{-}C_6)$ alkoxy, $(C_1\text{-}C_6)$ alkylthio, a conjugate, NR^3R^4, SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

wherein R^5 is hydrogen, a conjugate, $(C_1\text{-}C_6)$alkyl, hydroxy-, alkoxy-, or alkylthio-substituted $(C_1\text{-}C_6)$alkyl; and

R^3 and R^4 independently are hydrogen, a conjugate, $(C_1\text{-}C_4)$alkyl, hydroxy- or alkoxy- or alkylthio-substituted $(C_1\text{-}C_4)$alkyl, hydroxy, alkoxy, alkylthio or amino;

D and D_m independently are $(CR^6R^7)_z$;

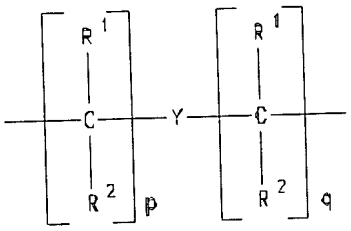
each of y and z is zero or an integer from 1 to 10, wherein the sum y + z is greater than 2 but not more than 10;

G_m is independently $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$, or $-NR^3SO_2-$ in either orientation;

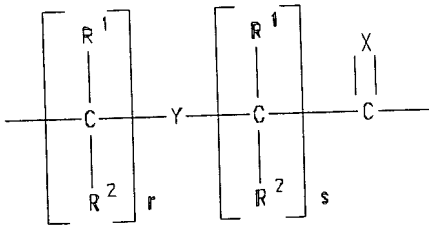
each pair of $A-A_m$ and $B-B_m$ are selected such that:

(a) A or A_m is a group of formula (IIa), (IIb) or (IIc) and B or B_m is N or R^3N+; or

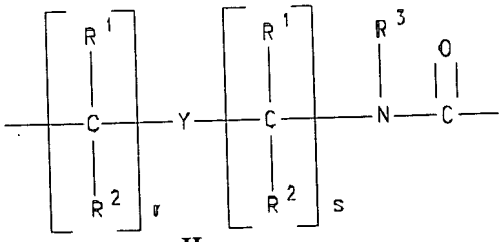
(b) A or A_m is a group of formula (IId) and B or B_m is CH;



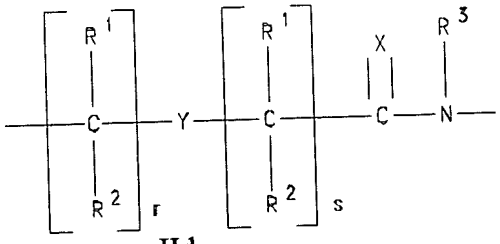
IIa



IIb



IIc



IId

where:

X is O, S, Se, NR^3, CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4;

each of p and q is zero or an integer from 1 to 5;

each of r and s is zero or an integer from 1 to 5;

R^1 and R^2 independently are hydrogen, (C_1-C_4)alkyl, hydroxy-substituted (C_1-C_4)alkyl, alkoxy-substituted (C_1-C_4)alkyl, alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

I is $-NR^8R^9$ or $-NR^{10}C(O)R^{11}$; wherein:

R^8, R^9, R^{10} and R^{11} independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer or a conjugate;

Q is $-CO_2H$, $-CO_2R^8$, $-CO_2R^9$, $-CONR^8R^9$, $-SO_3H$, $-SO_2NR^{10}R^{11}$ or an activated derivative of $-CO_2H$ or $-SO_3H$; and

wherein:

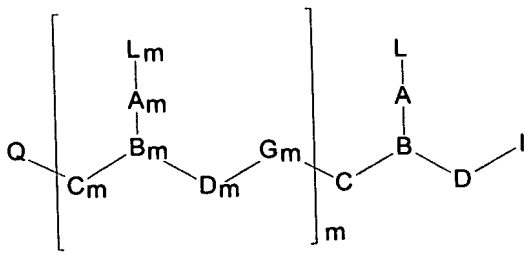
at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A, A_m, L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety; and

wherein when said Q or I is a crosslinking agent, said crosslinking agent is not lysine.

39. A peptide nucleic acid conjugate of the formula:



wherein:

m is an integer from 1 to about 50;

L and L_m independently are $R^{12}(R^{13})_a$ wherein:

R^{12} is hydrogen, hydroxy, (C_1-C_4)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate;

provided that at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13}, if present, is a conjugate; and

a is 0 or 1;

C and C_m independently are $(CR^6R^7)_y$; wherein:

R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4, SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

wherein R^5 is hydrogen, a conjugate, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6)alkyl; and

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio or amino;

D and D_m independently are $(CR^6R^7)_z$;

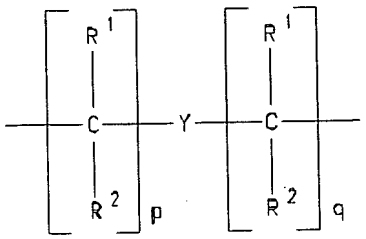
each of y and z is zero or an integer from 1 to 10, wherein the sum y + z is greater than 2 but not more than 10;

G_m is independently $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$, or $-NR^3SO_2-$ in either orientation;

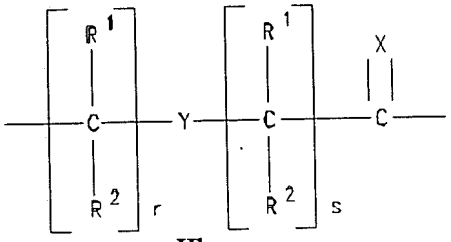
each pair of A-A_m and B-B_m are selected such that:

(a) A or A_m is a group of formula (IIa), (IIb) or (IIc) and B or B_m is N or R^3N^+; or

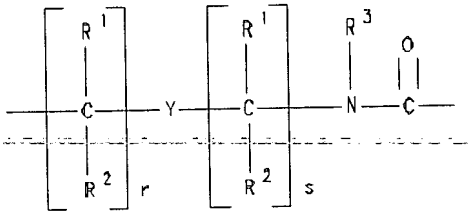
(b) A or A_m is a group of formula (IId) and B or B_m is CH;



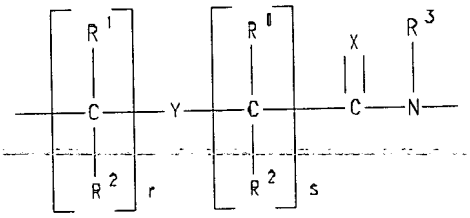
IIa



IIb



IIc



IId

wherein:

X is O, S, Se, NR^3, CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4;

each of p and q is zero or an integer from 1 to 5;

each of r and s is zero or an integer from 1 to 5;

R^1 and R^2 independently are hydrogen, $(C_1$-$C_4)$alkyl, hydroxy-substituted $(C_1$-$C_4)$alkyl, alkoxy-substituted $(C_1$-$C_4)$alkyl, alkylthio-substituted $(C_1$-$C_4)$alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

I is $-NR^8R^9$ or $-NR^{10}C(O)R^{11}$; wherein:

R^8, R^9, R^{10} and R^{11} independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer or a conjugate;

Q is $-CO_2H$, $-CO_2R^8$, $-CO_2R^9$, $-CONR^8R^9$, $-SO_3H$, $-SO_2NR^{10}R^{11}$ or an activated derivative of $-CO_2H$ or $-SO_3H$; and

wherein:

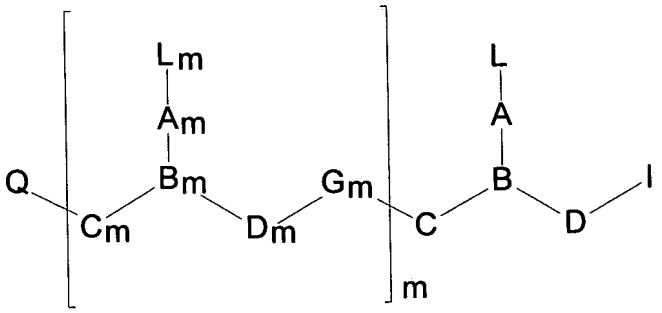
at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A, A_m, L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety; and

wherein at least one of R^1, R^2 or R^3 is a conjugate.

40. A peptide nucleic acid conjugate of the formula:



wherein:

m is an integer from 1 to about 50;

L and L_m independently are $R^{12}(R^{13})_a$ wherein:

R^{12} is hydrogen, hydroxy, (C_1-C_4)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate;

provided that at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13}, if present, is a conjugate; and

a is 0 or 1;

C and C_m independently are $(CR^6R^7)_y$; wherein:

R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4, SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

wherein R^5 is hydrogen, a conjugate, $(C_1\text{-}C_6)$alkyl, hydroxy-, alkoxy-, or alkylthio-substituted $(C_1\text{-}C_6)$alkyl; and

R^3 and R^4 independently are hydrogen, a conjugate, $(C_1\text{-}C_4)$alkyl, hydroxy- or alkoxy- or alkylthio-substituted $(C_1\text{-}C_4)$alkyl, hydroxy, alkoxy, alkylthio or amino;

D and D_m independently are $(CR^6R^7)_z$;

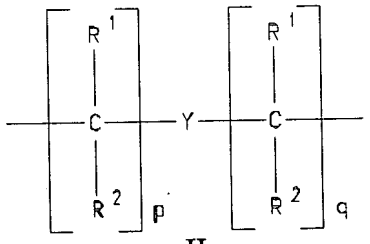
each of y and z is zero or an integer from 1 to 10, wherein the sum y + z is greater than 2 but not more than 10;

G_m is independently $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$, or $-NR^3SO_2-$ in either orientation;

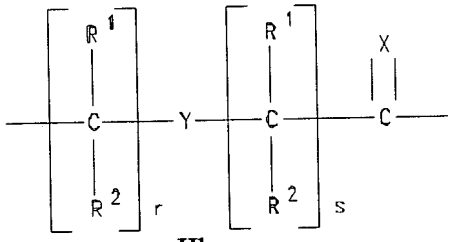
each pair of A-A_m and B-B_m are selected such that:

(a) A or A_m is a group of formula (IIa), (IIb) or (IIc) and B or B_m is N or R^3N^+; or

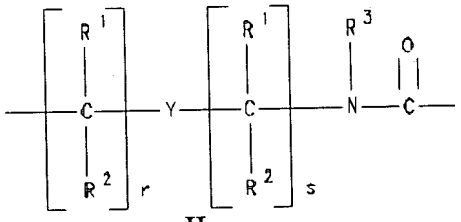
(b) A or A_m is a group of formula (IId) and B or B_m is CH;



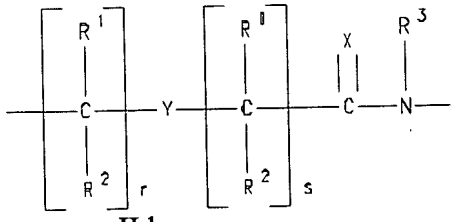
IIa



IIb



IIc



IId

wherein:

X is O, S, Se, NR^3, CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4;

each of p and q is zero or an integer from 1 to 5;

each of r and s is zero or an integer from 1 to 5;

R^1 and R^2 independently are hydrogen, (C_1-C_4)alkyl, hydroxy-substituted (C_1-C_4)alkyl, alkoxy-substituted (C_1-C_4)alkyl, alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

I is $-NR^8R^9$ or $-NR^{10}C(O)R^{11}$; wherein:

R^8, R^9, R^{10} and R^{11} independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer or a conjugate;

Q is $-CO_2H$, $-CO_2R^8$, $-CO_2R^9$, $-CONR^8R^9$, $-SO_3H$, $-SO_2NR^{10}R^{11}$ or an activated derivative of $-CO_2H$ or $-SO_3H$; and

wherein:

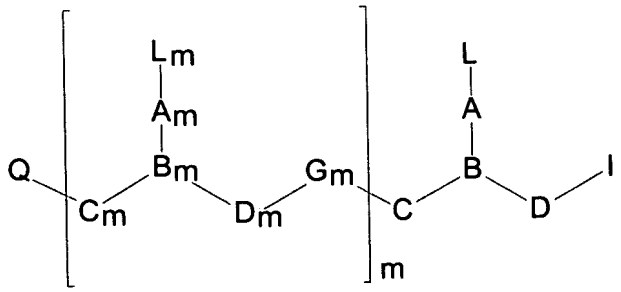
at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A, A_m, L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety; and

wherein at least one of R^8, R^9, R^{10} and R^{11} is a conjugate.

41. A peptide nucleic acid conjugate of the formula:



wherein:

m is an integer from 1 to about 50;

L and L_m independently are $R^{12}(R^{13})_a$ wherein:

R^{12} is hydrogen, hydroxy, (C_1-C_4)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate;

provided that at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13}, if present, is a conjugate; and

a is 0 or 1;

C and C_m independently are $(CR^6R^7)_y$; wherein:

R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4, SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

wherein R^5 is hydrogen, a conjugate, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C_1-C_6)alkyl; and

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio or amino;

D and D_m independently are $(CR^6R^7)_z$;

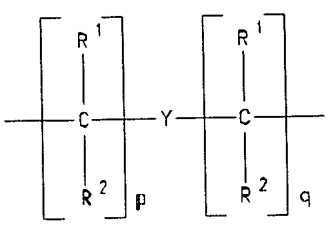
each of y and z is zero or an integer from 1 to 10, wherein the sum y + z is greater than 2 but not more than 10;

G_m is independently $-NR^3CO-$, $-NR^3CS-$, $-NR^3SO-$, or $-NR^3SO_2-$ in either orientation;

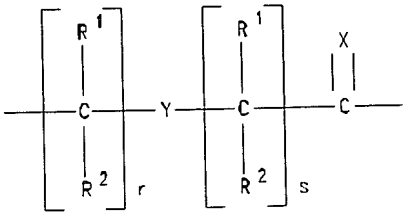
each pair of A-A_m and B-B_m are selected such that:

(a) A or A_m is a group of formula (IIa), (IIb) or (IIc) and B or B_m is N or R^3N^+; or

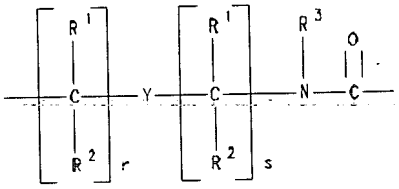
(b) A or A_m is a group of formula (IId) and B or B_m is CH;



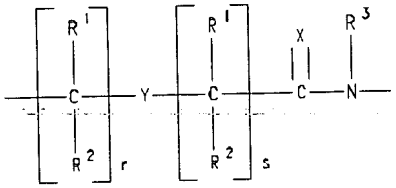
IIa



IIb



IIc



IId

wherein:

X is O, S, Se, NR^3, CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4;

each of p and q is zero or an integer from 1 to 5;

each of r and s is zero or an integer from 1 to 5;

R^1 and R^2 independently are hydrogen, $(C_1$-$C_4)$alkyl, hydroxy-substituted $(C_1$-$C_4)$alkyl, alkoxy-substituted $(C_1$-$C_4)$alkyl, alkylthio-substituted $(C_1$-$C_4)$alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

I is $-NR^8R^9$ or $-NR^{10}C(O)R^{11}$; wherein:

R^8, R^9, R^{10} and R^{11} independently are hydrogen, alkyl, an amino protecting group, a reporter ligand, an intercalator, a chelator, a peptide, a protein, a carbohydrate, a lipid, a steroid, a nucleoside, a nucleotide, a nucleotide diphosphate, a nucleotide triphosphate, an oligonucleotide, an oligonucleoside, a soluble polymer, a non-soluble polymer or a conjugate;

Q is $-CO_2H$, $-CO_2R^8$, $-CO_2R^9$, $-CONR^8R^9$, $-SO_3H$, $-SO_2NR^{10}R^{11}$ or an activated derivative of $-CO_2H$ or $-SO_3H$; and

wherein:

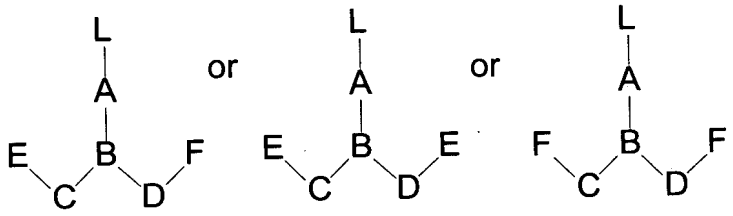
at least one of Q and I comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A, A_m, L, and L_m comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety; and

wherein at least one of R^3 R^4, R^5, R^6 and R^7 is a conjugate.

42. A peptide nucleic acid conjugate of formula:



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, $(C_1$-$C_4)$alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

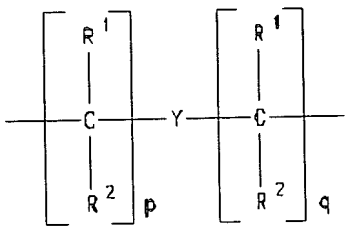
R^{13}, if present, is a conjugate; and

a is 0 or 1;

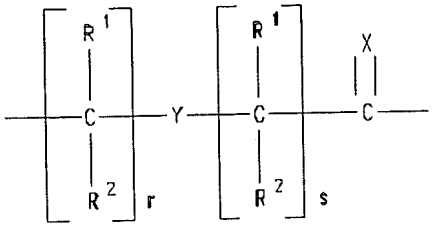
A and B are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+; or

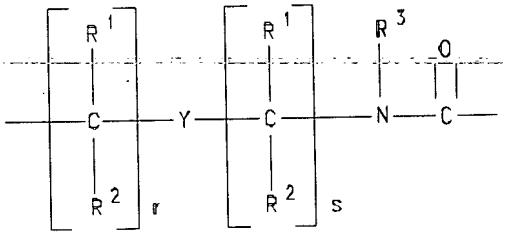
(b) A is a group of formula (IId) and B is CH;



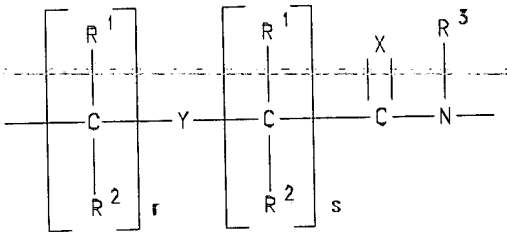
IIa



IIb



IIc



IId

where:

X is O, S, Se, NR^3, CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R^1 and R^2 independently are hydrogen, $(C_1\text{-}C_4)$alkyl, hydroxy-substituted $(C_1\text{-}C_4)$alkyl, alkoxy-substituted $(C_1\text{-}C_4)$alkyl, alkylthio-substituted $(C_1\text{-}C_4)$alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is $(CR^6R^7)_y$;

D is $(CR^6R^7)_z$; wherein:

R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2\text{-}C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1\text{-}C_6)$ alkoxy, $(C_1\text{-}C_6)$ alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, $(C_1\text{-}C_4)$alkyl, hydroxy- or alkoxy- or alkylthio-substituted $(C_1\text{-}C_4)$alkyl, hydroxy, alkoxy, alkylthio or amino; and

R^5 is hydrogen, a conjugate, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6)alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO_2OH or an activated or protected derivative thereof;

F independently is NHR^3 or $NPgR^3$, where Pg is an amino protecting group; or

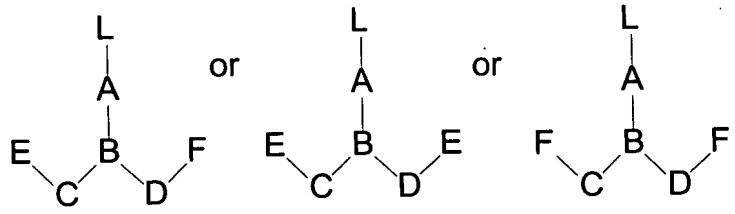
F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and

wherein said conjugate optionally includes a linking moiety; and

wherein at least one group R^3 is a conjugate.

43. A peptide nucleic acid conjugate of formula:



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, (C_1-C_4)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a

naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

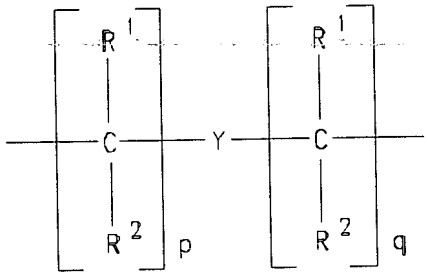
R^{13}, if present, is a conjugate; and

a is 0 or 1;

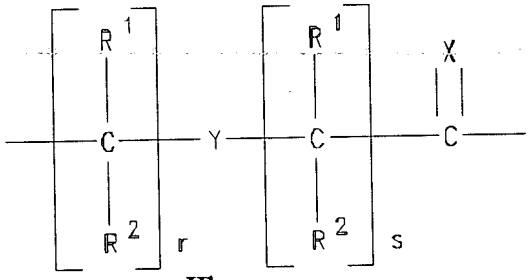
A and B are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+; or

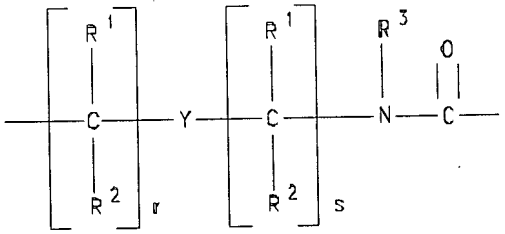
(b) A is a group of formula (IId) and B is CH;



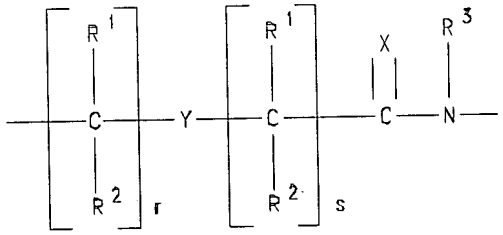
IIa



IIb



IIc



IId

where:

X is O, S, Se, NR^3, CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R^1 and R^2 independently are hydrogen, (C_1-C_4)alkyl, hydroxy-substituted (C_1-C_4)alkyl, alkoxy-substituted (C_1-C_4)alkyl, alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is $(CR^6R^7)_y$;

D is $(CR^6R^7)_z$; wherein:

R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio or amino; and

R^5 is hydrogen, a conjugate, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C_1-C_6)alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO_2OH or an activated or protected derivative thereof;

F independently is NHR^3 or $NPgR^3$, where Pg is an amino protecting group; or

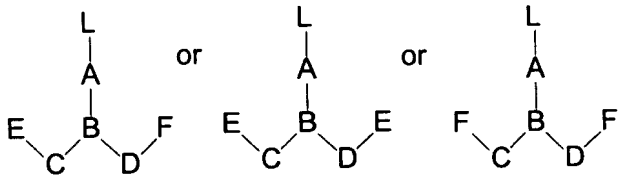
F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and

wherein said conjugate optionally includes a linking moiety; and

wherein at least one of said groups A or said groups B include a conjugate.

44. A peptide nucleic acid conjugate of formula:



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, $(C_1\text{-}C_4)$alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

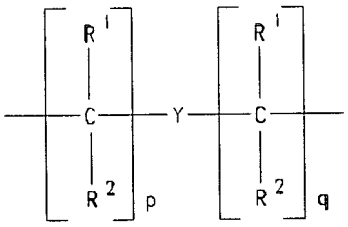
R^{13}, if present, is a conjugate; and

a is 0 or 1;

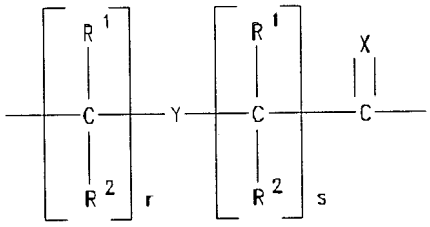
A and B are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+; or

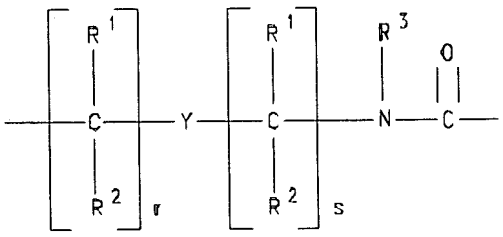
(b) A is a group of formula (IId) and B is CH;



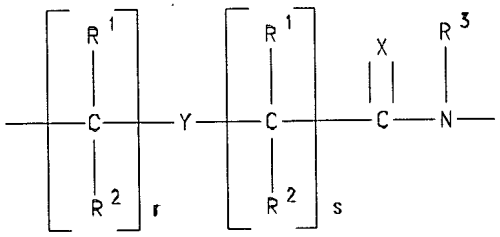
IIa



IIb



IIc



IId

where:

X is O, S, Se, NR^3, CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R^1 and R^2 independently are hydrogen, (C_1-C_4)alkyl, hydroxy-substituted (C_1-C_4)alkyl, alkoxy-substituted (C_1-C_4)alkyl, alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is $(CR^6R^7)_y$;

D is $(CR^6R^7)_z$; wherein:

R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio or amino; and

R^5 is hydrogen, a conjugate, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6)alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO_2OH or an activated or protected derivative thereof;

F independently is NHR^3 or $NPgR^3$, where Pg is an amino protecting group; or

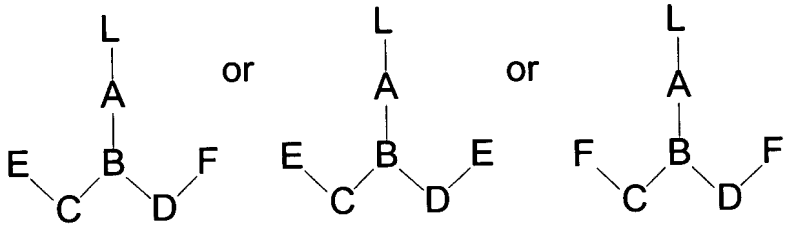
F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and

wherein said conjugate optionally includes a linking moiety; and

wherein at least one of group R^1 or group R^2 is a conjugate.

45. A peptide nucleic acid conjugate of formula:



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, (C_1-C_4)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

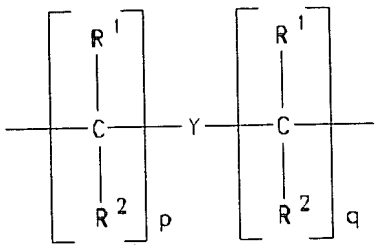
R^{13}, if present, is a conjugate; and

a is 0 or 1;

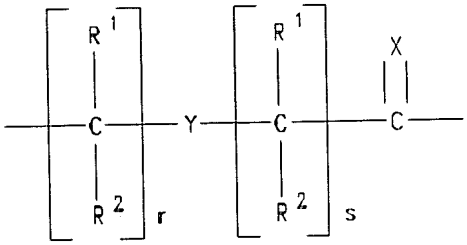
A and B are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+; or

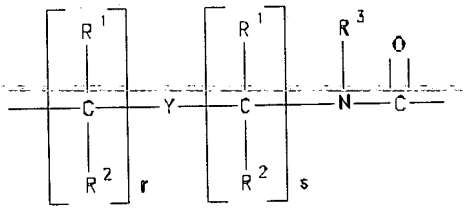
(b) A is a group of formula (IId) and B is CH;



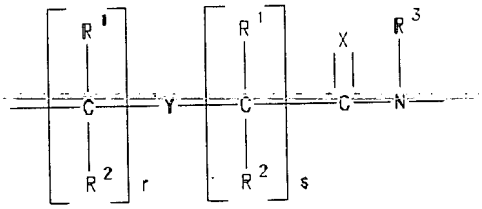
IIa



IIb



IIc



IId

where:

X is O, S, Se, NR^3, CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R^1 and R^2 independently are hydrogen, $(C_1\text{-}C_4)$alkyl, hydroxy-substituted $(C_1\text{-}C_4)$alkyl, alkoxy-substituted $(C_1\text{-}C_4)$alkyl, alkylthio-substituted $(C_1\text{-}C_4)$alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is $(CR^6R^7)_y$;

D is $(CR^6R^7)_z$; wherein:

R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2\text{-}C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1\text{-}C_6)$ alkoxy, $(C_1\text{-}C_6)$ alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, $(C_1\text{-}C_4)$alkyl, hydroxy- or alkoxy- or alkylthio-substituted $(C_1\text{-}C_4)$alkyl, hydroxy, alkoxy, alkylthio or amino; and

R^5 is hydrogen, a conjugate, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio- substituted (C_1-C_6)alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO_2OH or an activated or protected derivative thereof;

F independently is NHR^3 or $NPgR^3$, where Pg is an amino protecting group; or

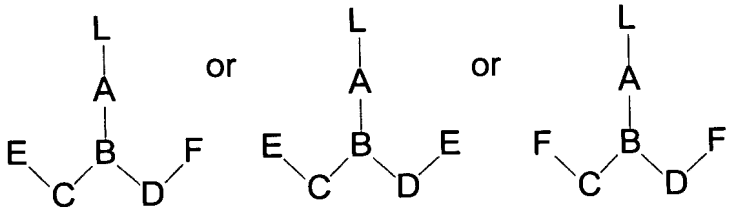
F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and

wherein said conjugate optionally includes a linking moiety; and

wherein at least one of R^3, R^4, R^5, R^6, and R^7 is a conjugate.

46. A peptide nucleic acid conjugate of formula:



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, (C_1-C_4)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at

least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

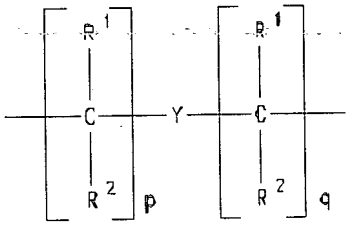
R^{13}, if present, is a conjugate; and

a is 0 or 1;

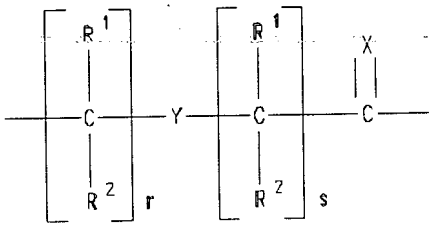
A and B are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+; or

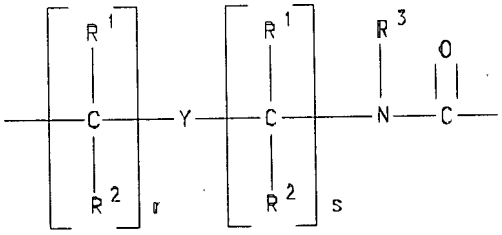
(b) A is a group of formula (IId) and B is CH;



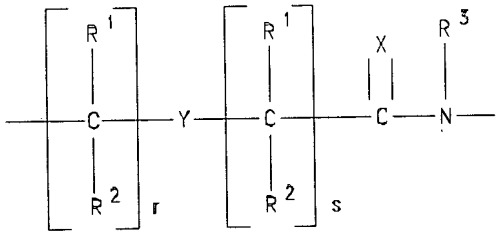
IIa



IIb



IIc



IId

where:

X is O, S, Se, NR^3, CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R^1 and R^2 independently are hydrogen, $(C_1\text{-}C_4)$alkyl, hydroxy-substituted $(C_1\text{-}C_4)$alkyl, alkoxy-substituted $(C_1\text{-}C_4)$alkyl, alkylthio-substituted $(C_1\text{-}C_4)$alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is $(CR^6R^7)_y$;

D is $(CR^6R^7)_z$; wherein:

R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio or amino; and

R^5 is hydrogen, a conjugate, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6)alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO_2OH or an activated or protected derivative thereof;

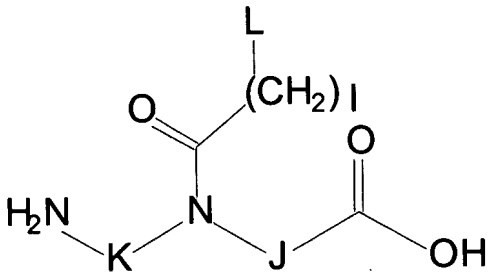
F independently is NHR^3 or $NPgR^3$, where Pg is an amino protecting group; or

F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

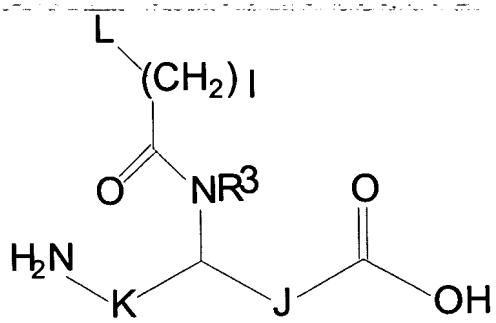
at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and wherein said conjugate optionally includes a linking moiety; and

wherein at least one of said groups C or said groups D include a conjugate.

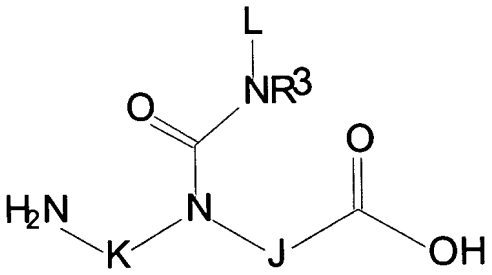
47. A peptide nucleic acid conjugate oligomer comprising a plurality of covalently linked PNA monomers wherein at least one of said PNA monomers has the formula:



or the formula



or the formula



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, $(C_1\text{-}C_4)$alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13}, if present, is a conjugate; and

a is 0 or 1;

K is $(CR^6R^7)_z$;

J is $(CR^6R^7)_y$; wherein:

R^6 and R^7 are independently hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio or amino;

R^5 is hydrogen, a conjugate, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6)alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

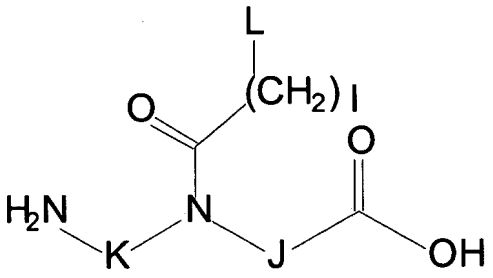
l is an integer from 1 to 5; and

at least one of L and R^3 comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

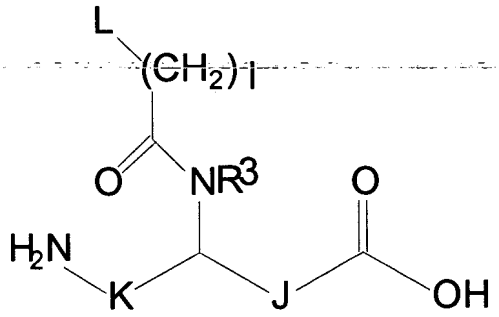
wherein said conjugate optionally includes a linking moiety; and

wherein at least one of R^3, R^4, R^5, R^6, and R^7 is a conjugate.

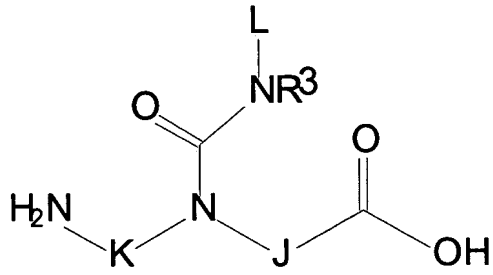
48. A peptide nucleic acid conjugate oligomer comprising a plurality of covalently linked PNA monomers wherein at least one of said PNA monomers has the formula:



or the formula



or the formula



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, $(C_1\text{-}C_4)$alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13}, if present, is a conjugate; and

a is 0 or 1;

K is $(CR^6R^7)_z$;

J is $(CR^6R^7)_y$; wherein:

R^6 and R^7 are independently hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2$-$C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1$-$C_6)$ alkoxy, $(C_1$-$C_6)$ alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, $(C_1$-$C_4)$alkyl, hydroxy- or alkoxy- or alkylthio-substituted $(C_1$-$C_4)$alkyl, hydroxy, alkoxy, alkylthio or amino;

R^5 is hydrogen, a conjugate, $(C_1$-$C_6)$alkyl, hydroxy-, alkoxy-, or alkylthio-substituted $(C_1$-$C_6)$alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

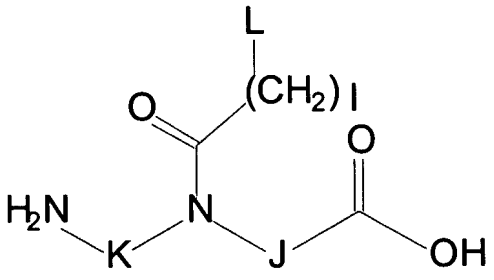
l is an integer from 1 to 5; and

at least one of L and R^3 comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

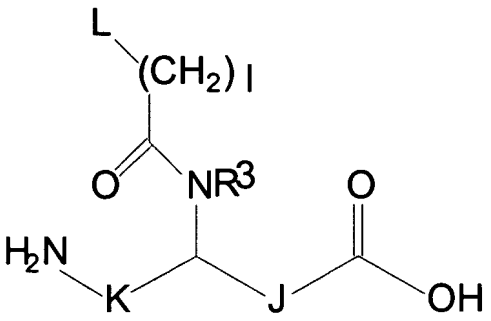
wherein said conjugate optionally includes a linking moiety; and

wherein at least one of said group K or said group J includes a conjugate.

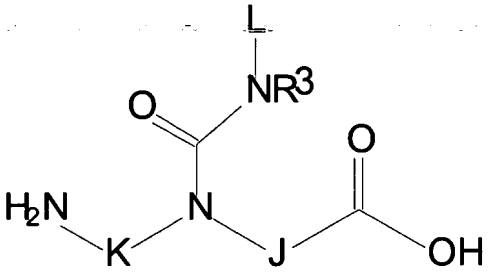
49. A peptide nucleic acid conjugate oligomer comprising a plurality of covalently linked PNA monomers wherein at least one of said PNA monomers has the formula:



or the formula



or the formula



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, $(C_1\text{-}C_4)$alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

R^{13}, if present, is a conjugate; and

a is 0 or 1;

K is $(CR^6R^7)_z$;

J is $(CR^6R^7)_y$; wherein:

R^6 and R^7 are independently hydrogen, a side chain of a naturally occurring alpha amino acid, $(C_2\text{-}C_6)$ alkyl, aryl, aralkyl, heteroaryl, hydroxy, $(C_1\text{-}C_6)$ alkoxy, $(C_1\text{-}C_6)$ alkylthio, a conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, $(C_1\text{-}C_4)$alkyl, hydroxy- or alkoxy- or alkylthio-substituted $(C_1\text{-}C_4)$alkyl, hydroxy, alkoxy, alkylthio or amino;

R^5 is hydrogen, a conjugate, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6)alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

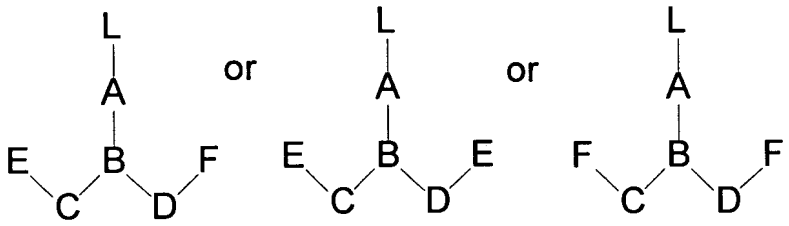
l is an integer from 1 to 5; and

at least one of L and R^3 comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers;

wherein said conjugate optionally includes a linking moiety; and

wherein said group R^3 is a conjugate.

50. A compound having one of the following formulas:



wherein:

L is $R^{12}(R^{13})_a$; wherein:

R^{12} is hydrogen, hydroxy, (C_1-C_4)alkanoyl, a naturally occurring nucleobase, a non-naturally occurring nucleobase, an aromatic moiety, a DNA intercalator, a nucleobase-binding group, a heterocyclic moiety, a reporter ligand, or a conjugate and at least one of R^{12} is a naturally occurring nucleobase, a non-naturally occurring nucleobase, a DNA intercalator, or a nucleobase-binding group;

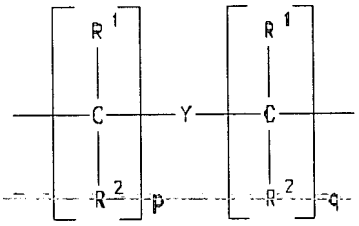
R^{13}, if present, is a conjugate; and

a is 0 or 1;

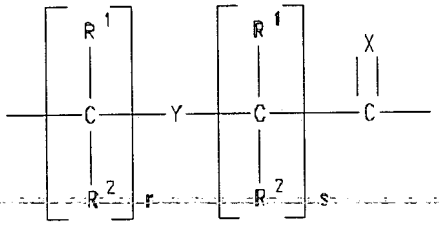
A and B are selected such that:

(a) A is a group of formula (IIa), (IIb) or (IIc) and B is N or R^3N^+; or

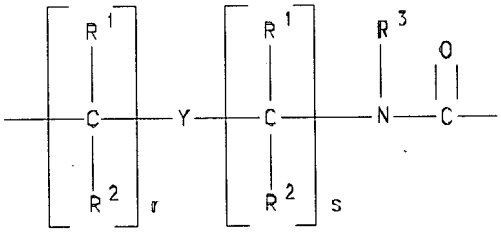
(b) A is a group of formula (IId) and B is CH;



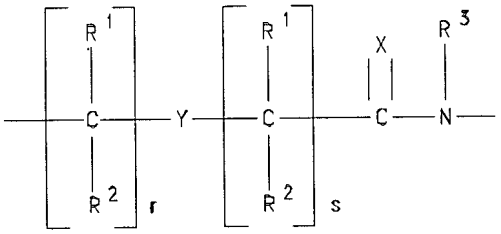
IIa



IIb



IIc



IId

where:

X is O, S, Se, NR^3, CH_2 or $C(CH_3)_2$;

Y is a single bond, O, S or NR^4;

p and q independently are zero or an integer from 1 to 5;

r and s independently are zero or an integer from 1 to 5;

R^1 and R^2 independently are hydrogen, (C_1-C_4)alkyl, hydroxy-substituted (C_1-C_4)alkyl, alkoxy-substituted (C_1-C_4)alkyl, alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio, amino, halogen or a conjugate;

C is $(CR^6R^7)_y$;

D is $(CR^6R^7)_z$; wherein:

R^6 and R^7 independently are hydrogen, a side chain of a naturally occurring alpha amino acid, (C_2-C_6) alkyl, aryl, aralkyl, heteroaryl, hydroxy, (C_1-C_6) alkoxy, (C_1-C_6) alkylthio, a

conjugate, NR^3R^4 and SR^5 or R^6 and R^7 taken together complete an alicyclic or heterocyclic system;

R^3 and R^4 independently are hydrogen, a conjugate, (C_1-C_4)alkyl, hydroxy- or alkoxy- or alkylthio-substituted (C_1-C_4)alkyl, hydroxy, alkoxy, alkylthio or amino; and

R^5 is hydrogen, a conjugate, (C_1-C_6)alkyl, hydroxy-, alkoxy-, or alkylthio-substituted (C_1-C_6)alkyl;

each of y and z is zero or an integer from 1 to 10, the sum y + z being greater than 2 but not more than 10;

E independently is COOH, CSOH, SOOH, SO_2OH or an activated or protected derivative thereof;

F independently is NHR^3 or $NPgR^3$, where Pg is an amino protecting group;

or

F comprises a conjugate selected from a terpene, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, a porphyrin, or an alkylator; or

at least one of A and L comprises a conjugate selected from a reporter enzyme, a reporter molecule, a steroid, a carbohydrate, a terpene, a peptide, a protein, a phospholipid, a cell receptor binding molecule, a crosslinking agent, a water soluble vitamin, a lipid soluble vitamin, an RNA/DNA cleaving complex, a metal chelator, a porphyrin, an alkylator, or a polymeric compound selected from polymeric amines, polymeric glycols and polyethers; and

wherein said conjugate optionally includes a linking moiety.

51. A peptide nucleic acid conjugate of claim 37 wherein one of Q or I comprises a conjugate, wherein said conjugate is polylysine.

52. A peptide nucleic acid conjugate of claim 37 wherein one of A, A_m, L or L_m comprises a conjugate, wherein said conjugate is polylysine.